

1 **What is claimed is:**

2 1. A method of producing humanized or human antibodies comprising:

3 (a) treating a transgenic non-human animal in which rearrangement of
4 immunoglobulin genes substantially stops early in life, engineered to express one or more
5 humanized or human immunoglobulin loci, with at least one antibody specific for the
6 endogenous surface IgM and/or IgD heavy and/or light chains produced by early B cells
7 of said animal, whereby early B cells expressing said surface IgM and/or IgD heavy
8 and/or light chains are depleted, and

9 (b) expressing said humanized or human immunoglobulin loci in said
10 animal.

1 2. The method of claim 1 wherein said animal relies substantially on gene
2 conversion and/or other mutational processes to create primary antibody diversity.

1 3. The method of claim 1 wherein said animal substantially stops antibody
2 diversification by gene rearrangement within the first month of its life.

1 4. The method of claim 1 wherein said animal is selected from the group
2 consisting of rabbits, birds, cows, pigs, sheep, goats and horses.

1 5. The method of claim 4 wherein said animal is selected from the group
2 consisting of rabbits, birds, cows and pigs.

1 6. The method of claim 5 wherein said animal is a transgenic rabbit or a
2 transgenic chicken expressing humanized or human immunoglobulin transgenes.

1 7. The method of claim 1 wherein said antibody is a polyclonal antibody
2 preparation.

1 8. The method of claim 7 wherein said polyclonal antibody preparation
2 comprises antibody fragments.

1 9. The method of claim 7 wherein said polyclonal antibody preparation is
2 injected into said animal during embryonic life or the first weeks of life.

- 1 10. The method of claim 7 wherein said polyclonal antibody preparation is
2 injected into said transgenic animal during the first two weeks of its life.
- 1 11. The method of claim 7 wherein said polyclonal antibody preparation is
2 injected into said transgenic animal during the first month of its life.
- 1 12. The method of claim 1 wherein said antibody is a monoclonal antibody.
- 1 13. The method of claim 12 wherein said antibody is an antibody fragment.
- 1 14. The method of claim 11 wherein more than one monoclonal antibody is
2 administered.
- 1 15. The method of any one of claims 1, 7, 8, 12 and 13, wherein said antibody
2 is conjugated to a toxin to form an immunotoxin.
- 1 16. A method for suppressing endogenous immunoglobulin expression in a
2 non-human animal comprising expressing in said animal one or more transgenes
3 encoding one or more antibodies specific for the endogenous surface IgM and/or IgD
4 heavy and/or light chains produced by early B cells of said non-human animal.
- 1 17. The method of claim 16 wherein said animal is a transgenic animal
2 expressing a human or humanized antibody.
- 1 18. The method of claim 17 wherein said transgenic animal is a non-rodent
2 animal.
- 1 19. The method of claim 18 wherein said non-rodent transgenic animal relies
2 substantially on gene conversion and/or other non-templated mutational processes to
3 create primary antibody repertoires.
- 1 20. The method of claim 18 wherein said transgenic non-rodent animal
2 substantially stops antibody diversification by gene rearrangement early in life.

1 21. The method of claim 20 wherein said transgenic non-rodent animal
2 substantially stops antibody diversification by gene rearrangement within the first month
3 of its life.

1 22. The method of claim 18 wherein said non-rodent transgenic animal is
2 selected from the group consisting of rabbits, birds, cows, pigs, sheep, goats and horses.

1 23. The method of claim 22 wherein said non-rodent transgenic animal is
2 selected from the group consisting of rabbits, birds, cows and pigs.

1 24. A method for producing a non-human, non-rodent transgenic animal in
2 which endogenous immunoglobulin production is suppressed, comprising treating said
3 non-human, non-rodent transgenic animal with at least one antibody specific for the
4 endogenous surface IgM and/or IgD heavy and/or light chains produced by early B cells
5 of said animal.

1 25. A method for producing a non-human transgenic animal in which
2 endogenous immunoglobulin production is suppressed, comprising expressing in said
3 non-human transgenic animal one or more transgenes encoding one or more antibodies
4 specific for the endogenous surface IgM and/or IgD heavy and/or light chains produced
5 by early B cells of said animal.

1 26. A non-human transgenic animal dominantly expressing human or
2 humanized antibodies, wherein said animal (1) uses primarily gene conversion and/or
3 other mutational processes to diversify the primary antibody repertoire; (2) expresses a
4 transgene comprising a human immunoglobulin gene or an immunoglobulin gene of said
5 animal modified to express at least part of a human immunoglobulin molecule, and (3)
6 expresses a transgene coding for one or several antibodies specific for endogenous
7 surface IgM and/or IgD heavy and/or light chains produced by early B cells of said
8 animal

1 27. The non-human transgenic animal of claim 26 which expresses one or
2 several transgenes coding for one or several monoclonal antibodies capable of
3 suppressing production of endogenous immunoglobulin μ or δ heavy and/or light chains.

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2 28. The non-human transgenic animal of claim 26 selected from the group
3 consisting of rabbits, birds, sheep, goat, pigs, cows and horses.